

REMARKS

Claims 1-7, 9-12, 14-35 and 47 are pending, and are presented for reconsideration. No amendments have been made to the claims.

Applicants gratefully acknowledge the Examiner's withdrawal of the rejection of pending claims over Stamm ('670) and Curtet ('726) .

Claims 1, 4-6, 9-12, 15-21, 23-35 and 47 are newly rejected under 35 U.S.C. §103(a) over U.S. Patent No. 4,800,079 to Boyer (Boyer '079) in view of Kiel EP 0 793 958 (EP 958), or EP 958 in view of Boyer '079. Boyer '079 issued January 24, 1989, and is assigned to Ethypharm, which also owns the instant application.

The Examiner acknowledges that Boyer '079 fails to teach a surfactant in a fenofibrate composition; but relies on EP 958 as teaching a fenofibrate composition comprising fenofibrate, surfactant and polyvinylpyrrolidone and other adjuvants, prepared by mixing, granulating and subsequent drying. The Examiner argues that it would have been obvious for one of ordinary skill in the art to combine Boyer '079 and EP 958.

This rejection is respectfully traversed. The rejection fails to present a *prima facie* case of obviousness for at least the reasons that one of ordinary skill in the art would not have been motivated to combine Boyer '079 and EP 958; and, even if combined, one would not have arrived at the claimed invention; and, even if the two references together suggest the claimed invention, they would not have suggested the surprising and unexpected results achieved.

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art,

to combine the teachings of the references. Second, there must be a reasonable expectation of success. Finally, the prior art references must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, not in applicant's disclosure. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Boyer '079 discloses the successive layering of an active agent on an inert core with the assistance of a binder. Specifically, an alcohol solution of a water-soluble (hydrophilic) binder is applied to the surface of an inert core. Dry, microcrystalline fenofibrate is then added to the tacky binder layer; and the binder is quickly dried. If the tacky binder layer is not quickly dried, the microcrystalline fenofibrate particles will deform, and lose the dissolution benefits associated with the microcrystalline fenofibrate. The layering of binder and fenofibrate is repeated until the requisite quantity of fenofibrate has been applied to the inert core. Lastly, the granules are coated with a protective layer. (See column 2, line 38 to column 3, line 12, of Boyer '079).

The rejection correctly acknowledged that Boyer '079 does not disclose the use of a surfactant, which is required by the present claims. But this is not the only difference. For example, various claims also require a specified weight ratio between fenofibrate and binding cellulose derivative (e.g., claim 21: "... comprising micronized fenofibrate, a surfactant, and a binding cellulose derivative as a solubilization agent, wherein the mass ratio of said fenofibrate to said binding cellulose derivative is between 5/1 and 15/1."). Such relationship is neither taught nor suggested by Boyer '079.

The rejection also mischaracterizes Boyer '079 in other respects. For example, the outer protective layer of Boyer does not form a matrix wherein the fenofibrate is deposited; the outer protective layer is applied over top of the layer of fenofibrate. In fact, it is the water-soluble binder material that serves as a matrix and, ultimately, a dispersant for the fenofibrate. Furthermore, in the example (Col. 3), the amount of fenofibrate is 75.5% rather than 80 %, as asserted.

EP 958 relies upon a process entirely distinct from that of Boyer '079; and produces a distinct product. EP 958 is limited to a fenofibrate formulation fabricated by wet granulation. The wet granulation method produces an irregular mixture lacking the finely layered structure of microcrystalline fenofibrate on an inert core, which is a characteristic of Boyer '079 and the present invention.

In EP 958, fenofibrate particles are mixed together simultaneously with polyvinylpyrrolidone particles, cross-linked polyvinylpyrrolidone particles, and, optionally, other adjuvant particles. There is no rapid drying. The EP 958 mixture is then granulated with an aqueous solution of surfactant(s), and the entire mixture is dried. See claim 1 and paragraph 0014, of EP 958.

The resulting product is quite different from the finely layered structure of Boyer 079. Boyer 079 requires a water soluble binder, and an iterative process of finely layered binder and fenofibrate followed by rapid drying (e.g., binder → fenofibrate → rapid drying; binder → fenofibrate ...) to minimize exposure of the microcrystalline fenofibrate to alcohol, which would otherwise destroy the microparticulate structure of fenofibrate. See, col. 2, line 64 – col. 3, line 23. Thus, the additives selected for use in the two methods would be expected to be quite different, and to play distinct roles.

In fact, EP 958 expressly distinguishes its process and product from the coated neutral cores of Boyer '079:

[0021] In contrast to EP-A1-256 933 [the EP equivalent of Boyer '079], according to which an application such as the spraying on of fenofibrate onto the polyvinylpyrrolidone acting solely as a binding agent is carried out, in the process of the invention a mixing of the fenofibrate with the polyvinylpyrrolidone and in addition with cross-linked polyvinylpyrrolidone takes place. There is also the difference from EP-A1-256 933, in which no cross-linked polyvinylpyrrolidone is used, which is even excluded according to its process, because a binding agent that is soluble in water must be used, that in the process of the invention cross-linked polyvinylpyrrolidone particles must be obligatorily also mixed in. A further difference resides in the fact that according to the process of the invention, in contrast to that of the cited publication, the granulation is performed with a surface-active agent in another stage.

EP 958 thus identifies at least four differences between its formulation and Boyer '079:

- Boyer '079 is directed to spray-coated neutral cores while EP 958 is directed to a mixture (i.e., wet granulation);
- Boyer '079 utilizes polyvinylpyrrolidone as the sole binding agent, while EP 958 utilizes both polyvinylpyrrolidone and cross-linked polyvinylpyrrolidone, the latter characterized as being essential ;
- Boyer '079 excludes the use of cross-linked polyvinylpyrrolidone because the binder therein must be hydrophilic, and cross-linked polyvinylpyrrolidone is not hydrophilic; and
- Boyer '079 does not utilize a surfactant, while EP 958 must utilize a surfactant.

Boyer '079 is directed to coated neutral cores, while EP 958 is directed to wet granulation. One of ordinary skill in the art would have recognized that finely layered

microcrystalline fenofibrate coated neutral cores and fenofibrate formulations from wet granulation are as apples and oranges – they are formed by different processes, using different additives that have different properties for different purposes. One of ordinary skill in the art would not have expected that ingredients used in wet granulation would have the same properties and impart the same benefits when used in coating neutral cores, nor would one have expected that products produced by the one are interchangeable with the other. The rejection does not identify any teaching or suggestion to the contrary.

Indeed, EP 958 expressly identifies some of those differences. One of ordinary skill in the art would have understood from EP 958 that materials said to be beneficial – perhaps even necessary - in a wet granulation formulation are not beneficial – and perhaps must be excluded – in a neutral core coated formulation. Thus, there is not only a lack of motivation to combine EP 958 and Boyer '079, but in fact the EP 958 reference itself contains an express teaching away from such a combination.

One of ordinary skill in the art would not have combined Boyer '079 and EP 958 as in the outstanding rejection; and, even if one had so combined those references, there is no showing that one would have arrived at the presently claimed invention, nor would there have been any reasonable expectation of achieving the present unexpected advantages, as described in the Bobotas Declarations. Accordingly, Applicants respectfully submit that the rejection does not present a *prima facie* case of obviousness based on these references. Applicants respectfully request withdrawal of the outstanding rejection of claims 1, 4-6, 9-12, 15-21, 23-35 and 47 under 35 U.S.C. §103(a) based on Boyer '079 and EP 958.

Claims 2, 3, 7, 14 and 22 are newly rejected under 35 U.S.C. §103(a) as being unpatentable over Boyer '079 in view of EP 958, as applied to claims 1, 4-6, 9-12, 15-21 and 23-35 above, and further in view of WO 96/01621. The Examiner acknowledges that neither Boyer '079 nor EP 958 teaches the specific polymer of the rejected claims. WO 621 is relied upon for disclosing the specific polymer.

As noted above, one of ordinary skill in the art would not have been motivated to combine the teachings of Boyer '079 and EP 958; and, even if one had so combined those references, there would not have been any reasonable expectation of success in achieving the benefits and advantages of the presently claimed invention. The addition of WO 621 does not overcome those deficiencies. Therefore, Applicants respectfully submit that the rejection of claims 2, 3, 7, 14 and 22 under 35 U.S.C. §103(a) should also be withdrawn.

Claims 1-7, 9-12, 14-35 and 47 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-45 of copending application Serial No. 10/677,861. Reconsideration of this rejection is respectfully requested for at least the following reasons.

Applicants submit that the claims of the present application and those of the '861 application are drawn to different inventions and are capable of supporting separate patents. Mere overlap in the scope of claims is not, *per se*, double patenting (M.P.E.P. § 804, page 800-19, right hand column).

Moreover, it is the policy of the Patent and Trademark Office to issue an earlier filed application where a provisional obviousness double patenting rejection is the only remaining issue (M.P.E.P. § 804, page 800-17, right hand column).

Claims 1-7, 9-12, 14-35 and 47 allegedly are directed to an invention not patentably distinct from claims 1-45 of commonly assigned application No. 10/677,861 for reasons set forth on page 7 of the Office Action. Respectfully, Applicants disagree and submit that the claims of the respective applications are drawn to patentably distinct inventions.

In view of the foregoing amendments and remarks, applicants respectfully request reconsideration and withdrawal of all outstanding rejections. Applicants submit that the claims are now in condition for allowance, and respectfully request formal notification to that effect. If, however, the Examiner perceives any impediments to such a notice of allowability, whether substantive or formal, the Examiner is encouraged to call Applicants' attorney at the number provided below. Such informal communication will expedite examination and disposition of this case.

Respectfully submitted,

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Date: April 13, 2006

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